Efficacy and safety profiles of manidipine compared with amlodipine: a meta-analysis of head-to-head trials

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CRD summary
The review concluded that the efficacy/safety profile of manidipine was superior to amlodipine in patients with hypertension. Potential for biases within the review and uncertain quality of the evidence base limits the reliability of the pooled results.

Authors’ objectives
To compare the efficacy and safety of manidipine versus amlodipine in patients with hypertension.

Searching
PREMEDLINE, MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from January 1995 to July 2009. A manual search of the literature and congress abstracts was undertaken. Leading authors were contacted for unpublished data.

Study selection
Randomised controlled trials (RCTs) of manidipine versus amlodipine in patients with hypertension were eligible for inclusion. Trials had to last at least one month and provide assessments of systolic and diastolic blood pressure reduction, global side-effects and ankle oedema using validated techniques.

The included trials studied 10mg to 20mg manidipine versus 5mg to 10mg amlodipine in patients with hypertension. Patient ages, where reported, ranged from 35 to 70 years. Trial duration ranged from 12 to 48 weeks. Loss to follow-up varied from 1.56% to 26%.

Two reviewers performed study selection.

Assessment of study quality
The authors did not state whether they performed formal validity assessment, although they stated that two authors considered double blinding.

Data extraction
Data were extracted on diastolic and systolic blood pressure and used to calculate effect sizes and 95% confidence intervals (CIs). Data on adverse events and ankle oedema were extracted and used to calculate relative risks (RRs) and risk differences (RDs), with 95% CIs.

The authors did not state how many reviewers performed data extraction.

Methods of synthesis
Fixed-effect meta-analysis was used to calculate pooled relative risks and risk differences, with 95% CIs. Random-effects meta-analysis was used to calculate pooled effect sizes for blood pressure outcomes. Statistical heterogeneity was assessed and deemed non-significant where p>0.10. Publication bias was assessed using funnel plots, Fail Safe N, regression intercept method and rank correlation.

Results of the review
Four RCTs (838 participants) were included in the review. Three trials were reported to be double blind.

There was no statistically significant difference in reduction in systolic or diastolic blood pressure with manidipine compared to amlodipine. Compared to amlodipine, manidipine had a statistically significantly lower risk of adverse events (RR 0.69, 95% CI 0.56 to 0.85) and ankle oedema (RR 0.35, 95% CI 0.23 to 0.54). There was evidence of statistical heterogeneity with blood pressure outcomes but not with adverse events or ankle oedema. There was no
evidence of significant publication bias.

**Authors' conclusions**
The efficacy/safety profile of manidipine was superior to amlodipine in patients with hypertension.

**CRD commentary**
Inclusion criteria for the review were clearly defined and several relevant data sources were searched. Search terms were not reported. Publication bias was assessed and was not detected, although the validity of the assessment with less than 10 trials was limited. Attempts were made to reduce reviewer error and bias during study selection but the authors did not state whether the same methods were used for data extraction. The authors did not state whether formal quality assessment was undertaken, however the authors acknowledged there were baseline differences across the trials.

Trials were combined using appropriate statistical methods. Statistical heterogeneity was assessed, but it was not fully reported.

Potential for biases within the review and uncertain quality of the evidence base limits the reliability of the pooled results.

**Implications of the review for practice and research**
**Practice:** The authors stated that the results of the review were important as patients who persisted with treatment had a greater chance of normalising their blood pressure, and thus reducing their risk of renal and cardiovascular events.

**Research:** The authors did not state any implications for research.

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Record Status
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